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L1 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2006 ACS on STN
RN **50-78-2** REGISTRY
ED Entered STN: 16 Nov 1984
CN Benzoic acid, 2-(acetyloxy)- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 2-(Acetyloxy)benzoic acid
CN 2-Acetoxybenzoic acid
CN 2-Carboxyphenyl acetate
CN A.S.A. Empirin
CN AC 5230
CN Acenterine
CN Acesal
CN Acesan
CN Acetard
CN Aceticyl
CN Acetilum acidulatum
CN Acetisal
CN Acetol
CN Acetonyl
CN Acetophen
CN Acetosal
CN Acetosalic acid
CN Acetosalin
CN Acetylin
CN Acetylsal
CN Acetylsalicylic acid
CN Acetyonyl
CN Acetysal
CN Acidum acetylsalicylicum
CN Acimetten
CN Acisal
CN Acylpyrin
CN Adiro
CN Albyl E
CN ASA
CN Asaflow
CN Asagran
CN Asatard
CN Ascoden 30
CN Ascolong
CN Ascriptin
CN Aspalon
CN Aspergum
CN Aspirdrops
CN Aspirin
CN Aspirin Protect 100
CN Aspirin Protect 300
CN Aspirin-Direkt
CN Aspirina 03
CN Aspro
CN Aspro Clear
CN Aspropharm
CN Asteric
CN Bayer
CN Benaspir
ADDITIONAL NAMES NOT AVAILABLE IN THIS FORMAT - Use FCN, FIDE, or ALL for DISPLAY
FS 3D CONCORD

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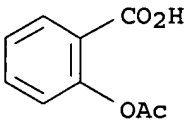
DR 11126-35-5, 11126-37-7, 98201-60-6, 2349-94-2, 26914-13-6
MF C9 H8 O4
CI COM
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, AQUIRE, BEILSTEIN*, BIOSIS, BIOTECHNO, CA, CABA, CAOLD, CAPLUS, CASREACT, CBNB, CHEMCATS, CHEMINFORMRX, CHEMLIST, CIN, CSCHEM, CSNB, DDFU, DETHERM*, DIOGENES, DIPPR*, DRUGU, EMBASE, GMELIN*, HSDB*, IFICDB, IFIPAT, IFIUDB, IMSCOSEARCH, IPA, MEDLINE, MRCK*, MSDS-OHS, NAPRALERT, NIOSHTIC, PATDPASPC, PDLCOM*, PHAR, PIRA, PROMT, PROUSDDR, PS, RTECS*, SPECINFO, SYNTHLINE, TOXCENTER, TULSA, ULIDAT, USAN, USPAT2, USPATFULL, VETU, VTB
(*File contains numerically searchable property data)
Other Sources: DSL**, EINECS**, TSCA**
(**Enter CHEMLIST File for up-to-date regulatory information)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

19680 REFERENCES IN FILE CA (1907 TO DATE)
383 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
19750 REFERENCES IN FILE CAPLUS (1907 TO DATE)
1 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

=> s 51803-78-2/rn
L2 1 51803-78-2/RN

=> d l2

L2 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2006 ACS on STN
RN **51803-78-2** REGISTRY
ED Entered STN: 16 Nov 1984
CN Methanesulfonamide, N-(4-nitro-2-phenoxyphenyl)- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 2-Phenoxy-4-nitromethanesulfonanilide
CN 4'-Nitro-2'-phenoxymethanesulfonanilide
CN 4-Nitro-2-phenoxymethanesulfonanilide
CN Aulin
CN Flogovital
CN Mesulid
CN Nimed
CN Nimepast
CN Nimesulide
CN Nimulid
CN Nise*Gel
CN Nisulid
CN Orthobid
CN R 805
CN R 805 (pharmaceutical)
CN Sulidene
FS 3D CONCORD
MF C13 H12 N2 O5 S
CI COM

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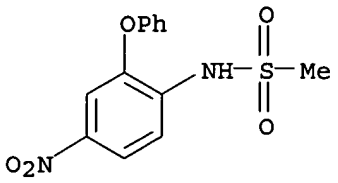
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOSIS, BIOTECHNO, CA, CAPLUS, CASREACT, CBNB, CHEMCATS, CHEMLIST, CIN, CSCHEM, DDFU, DETHERM*, DRUGU, EMBASE, IMSCOSEARCH, IMSDRUGNEWS, IMSPATENTS, IMSRESEARCH, IPA, MEDLINE, MRCK*, PHAR, PROMT, PROUSDDR, PS, RTECS*, SCISEARCH, SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL, VETU
(*File contains numerically searchable property data)
Other Sources: EINECS**, WHO
(**Enter CHEMLIST File for up-to-date regulatory information)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1043 REFERENCES IN FILE CA (1907 TO DATE)
31 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
1049 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> file medicine
FILE 'DRUGMONOG' ACCESS NOT AUTHORIZED

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	4.68	5.16

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FILE 'TOXCENTER' ENTERED AT 10:25:32 ON 21 FEB 2006

FILE 'USPATFULL' ENTERED AT 10:25:32 ON 21 FEB 2006

FILE 'USPAT2' ENTERED AT 10:25:32 ON 21 FEB 2006


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L4       440667 ASPIRIN OR ASA OR ACETYLSALICYLIC ACID

=> s l3 or l4

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L5       444595 L3 OR L4

=> s l2 or nimesulide
'RN' IS NOT A VALID FIELD CODE
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L6        12543 L2 OR NIMESULIDE

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L7         2988 L4 AND L6

=> s sub-therapeutic
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L8         2380 SUB-THERAPEUTIC

=> s l8 and l7
L9           19 L8 AND L7

=> s low dose
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L10      352538 LOW DOSE

=> s l8 or l10
  32 FILES SEARCHED...
L11      354769 L8 OR L10

=> s l7 and l11

  28 FILES SEARCHED...
L12         159 L7 AND L11

=> dup rem

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DUPLICATE IS NOT AVAILABLE IN 'ADISINSIGHT, ADISNEWS, DGENE, DRUGMONOG2,
IMSPRODUCT, KOSMET, NUTRACEUT, PCTGEN, PHARMAML'.
ANSWERS FROM THESE FILES WILL BE CONSIDERED UNIQUE
PROCESSING COMPLETED FOR L12
L13          132 DUP REM L12 (27 DUPLICATES REMOVED)

=> s synerg?
L14      749513 SYNERG?

=> s l13 and l14

  26 FILES SEARCHED...
L15          73 L13 AND L14
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=> d l15 70-73 ibib, kwic

L15 ANSWER 70 OF 73 USPATFULL on STN
ACCESSION NUMBER: 2002:88001 USPATFULL
TITLE: Opioid agonist/opioid antagonist/acetaminophen combinations
INVENTOR(S): Kaiko, Robert F., Weston, CT, United States
Colucci, Robert D., Newtown, CT, United States
PATENT ASSIGNEE(S): Euro-Celtique, S.A., Luxembourg, LUXEMBOURG (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6375957	B1	20020423
APPLICATION INFO.:	US 2000-503020		20000211 (9)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 1998-218662, filed on 22 Dec 1998

	NUMBER	DATE
PRIORITY INFORMATION:	US 1997-68480P	19971222 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: GRANTED
PRIMARY EXAMINER: Page, Thurman K.
ASSISTANT EXAMINER: Ware, Todd D
LEGAL REPRESENTATIVE: Davidson, Davidson & Kappel, LLC
NUMBER OF CLAIMS: 55
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 19 Drawing Figure(s); 12 Drawing Page(s)
LINE COUNT: 2580
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUMM . . . 21:162-8, studied the combination of naloxone 0.25 mg and Percodan® (composed of 4.5 mg oxycodone HCl, oxycodone terephthalate 0.28 mg, **aspirin** 224 mg, phenacetin 160 mg, and caffeine 32 mg) compared to Percodan® alone, and placebo in a crossover study of. . .

SUMM . . . also included, in addition to the opioid antagonist. Such non-opioid drugs would preferably provide additional analgesia, and include, for example, **aspirin**, acetaminophen, non-steroidal antiinflammatory drugs ("NSAIDS"), NMDA antagonists, and cycooxygenase-II inhibitors ("COX-II inhibitors"). In yet further embodiments, a non-opioid drug can. . .

DETD . . . hydrocodone bitartrate is commercially available in the United States only as a fixed combination with non-opiate drugs (i.e., ibuprofen, acetaminophen, **aspirin**, etc.) for relief of moderate or moderately severe pain.

DETD . . . mg hydrocodone bitartrate and 650 mg acetaminophen; and 7.5 mg hydrocodone bitartrate and 750 mg acetaminophen. Hydrocodone in combination with **aspirin** is given in an oral dosage form to adults generally in 1-2 tablets every 4-6 hours as needed to alleviate pain. The tablet form is 5 mg hydrocodone bitartrate and 224 mg **aspirin** with 32 mg caffeine; or 5 mg hydrocodone bitartrate and 500 mg **aspirin**. A relatively new formulation comprises hydrocodone bitartrate and ibuprofen. Vicoprofen®, commercially available in the U.S. from Knoll Laboratories, is a. . .

DETD It is known that acetaminophen can act **synergistically** with certain opioids. For example, U.S. Pat. No. 5,336,691 (Raffa, et al.), hereby incorporated by reference, describes formulations which include. . . the components of the compositions are within certain ratios the

pharmacological effects of the compositions are said to be superadditive (**synergistic**). A. Pircio et al., Arch. Int. Pharmacodyn., 235, 116 (1978) report superadditive analgesia with a 1:125 mixture of butorphanol, an. . .

DETD In certain embodiments, the invention allows for the use of lower doses of the opioid analgesic or acetaminophen (apparent one-way **synergy**), or lower doses of both drugs (two-way **synergy**) than would normally be required when either drug is used alone. By using lower amounts of either or both drugs,. . .

DETD . . . dose of opioid analgesic alone. In such embodiments, the combinations display what is referred to herein as an "apparent one-way **synergy**", meaning that the dose of acetaminophen potentiates the effect of the opioid analgesic, but the dose of opioid analgesic does. . . the potentiation exhibited between the acetaminophen and the opioid analgesic is such that the dosage of opioid analgesic would be **sub-therapeutic** if administered without the dosage of acetaminophen. In other preferred embodiments, the present invention relates to a pharmaceutical composition comprising. . .

DETD . . . between the drugs, and the analgesia derived from the combination of drugs in reduced doses is surprisingly enhanced. The two-way **synergism** is not always readily apparent in actual dosages due to the potency ratio of the opioid analgesic to the acetaminophen. . .

DETD . . . invention is also directed to a method for providing effective pain management in humans, comprising administering an analgesically effective or **sub-therapeutic** amount of an opioid analgesic; an opioid antagonist in a fashion as described herein; and administering an effective amount of. . .

DETD . . . the opioid analgesic and opioid antagonist, or the opioid analgesic/opioid antagonist/acetaminophen combination, which additional drug(s) may or may not act **synergistically** with any or all of these drugs. Thus, in certain embodiments, a combination of two opioid analgesics may be included. . . also included, in addition to the opioid antagonist. Such non-opioid drugs would preferably provide additional analgesia, and include, for example, **aspirin**; acetaminophen; non-sterioidal antiinflammatory drugs ("NSAIDS"), e.g., ibuprofen, ketoprofen, etc.; N-methyl-D-aspartate (NMDA) receptor antagonists, e.g., a morphinan such as dextromethorphan or. . .

DETD . . . opioid agonist/opioid antagonist, or combinations of opioid agonist/opioid antagonist/acetaminophen as disclosed herein, which agents may or may not provide additive, **synergistic** (superadditive) effects. The invention allows for the use of lower doses of the opioid analgesic by virtue of the inclusion. . .

DETD . . . Certain preferred COX-2 inhibitors include celecoxib (SC-58635), DUP-697, flosulide (CGP-28238), meloxicam, 6-methoxy-2 naphthylacetic acid (6-MNA), MK-966, nabumetone (prodrug for 6-MNA), **nimesulide**, NS-398, SC-5766, SC-58215, T-614; or combinations thereof. Dosage levels of COX-2 inhibitor on the order of from about 0.005 mg. . .

DETD . . . incorporated by reference, describes formulations for the treatment of pain in which the drug olanzapine is said to provide a **synergistic** effect when administered with one or more drugs useful in the treatment of pain (including acetaminophen and opioids). U.S. Pat.. . . describes formulations for the treatment of pain in which certain phenyl oxazoles or phenyl thiazoles are said to provide a **synergistic** effect when administered with one or more drugs useful in the treatment of pain (including acetaminophen and opioids).

DETD . . . agents which may provide additional benefits to the dosage forms of the invention, whether it be to provide additive or

synergistic analgetic effects, or treatment of additional conditions, are deemed encompassed by this disclosure and the appended claims.

CLM What is claimed is:

. . . form of claim 1, further comprising an additional non-opioid drug selected from the group consisting of a COX-2 inhibitor and **aspirin**.

L15 ANSWER 71 OF 73 USPATFULL on STN

ACCESSION NUMBER:	2002:48606 USPATFULL
TITLE:	Irrigation solution and method for inhibition of pain and inflammation
INVENTOR(S):	Demopulos, Gregory A., Mercer Island, WA, UNITED STATES Pierce-Palmer, Pamela, San Francisco, CA, UNITED STATES Herz, Jeffrey M., Mill Creek, WA, UNITED STATES
PATENT ASSIGNEE(S):	Omeros Medical Systems (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2002028798	A1	20020307
APPLICATION INFO.:	US 2001-839633	A1	20010420 (9)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. WO 1999-US24625, filed on 20 Oct 1999, UNKNOWN Continuation-in-part of Ser. No. WO 1999-US24672, filed on 20 Oct 1999, UNKNOWN Continuation-in-part of Ser. No. WO 1999-US24558, filed on 20 Oct 1999, UNKNOWN Continuation-in-part of Ser. No. WO 1999-US24557, filed on 20 Oct 1999, UNKNOWN Continuation-in-part of Ser. No. WO 1999-US26330, filed on 5 Nov 1999, UNKNOWN Continuation-in-part of Ser. No. US 1998-72913, filed on 4 May 1998, UNKNOWN Continuation of Ser. No. US 1996-670699, filed on 26 Jun 1996, UNKNOWN Continuation-in-part of Ser. No. WO 1995-US16028, filed on 12 Dec 1995, UNKNOWN Continuation-in-part of Ser. No. US 1994-353775, filed on 12 Dec 1994, ABANDONED

	NUMBER	DATE
PRIORITY INFORMATION:	US 1998-105026P	19981020 (60)
	US 1998-105029P	19981020 (60)
	US 1998-105044P	19981020 (60)
	US 1998-105166P	19981021 (60)
	US 1998-107256P	19981105 (60)

DOCUMENT TYPE:	Utility
FILE SEGMENT:	APPLICATION
LEGAL REPRESENTATIVE:	CHRISTENSEN, O'CONNOR, JOHNSON, KINDNESS, PLLC, 1420 FIFTH AVENUE, SUITE 2800, SEATTLE, WA, 98101-2347
NUMBER OF CLAIMS:	19
EXEMPLARY CLAIM:	1
NUMBER OF DRAWINGS:	12 Drawing Page(s)
LINE COUNT:	4713

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUMM . . . pp. 403-416 (1985). Combinations of these three agonists (5-HT, bradykinin and histamine) applied together have been demonstrated to display a **synergistic** pain-causing effect, producing a long-lasting and intense pain signal. Sicuteri et al., 1965; Richardson et al., 1985; Kessler, W., et. . .

SUMM . . . Levine, J. D., et al., Desipramine Enhances Opiate

Postoperative Analgesia, Pain 27, pp. 45-49 (1986); Kerrick, J. M., et al., **Low-Dose** Amitriptyline as an Adjunct to Opioids for Postoperative Orthopedic Pain: a Placebo-Controlled Trial Period, Pain 52, pp. 325-30 (1993). In. . .

SUMM . . . the activity of postoperatively released 5-HT in the second study. (3) Since multiple inflammatory mediators exist, and studies have demonstrated **synergism** between the inflammatory mediators, blocking only one agent (5-HT) may not sufficiently inhibit the inflammatory response to tissue injury.

SUMM [0019] The advantages of **low dose** applications of agents are three-fold. The most important is the absence of systemic side effects that often limit the usefulness. . .

SUMM . . . processes, including pain and inflammation, vasospasm, smooth muscle spasm and restenosis. The action of these agents is considered to be **synergistic**, in that the multiple receptor antagonists and inhibitory agonists of the present invention provide a disproportionately increased efficacy in combination relative to the efficacy of the individual agents. The **synergistic** action of several of the agents of the present invention are discussed, by way of example, below in the detailed. . .

DRWD . . . activity and calcium levels. LGR designates ligand-gated receptor, and MAPK designates mitogen-activated protein kinase. These interactions define the basis for **synergistic** interactions between molecular targets mediating spasm and restenosis. The GPCR signaling pathway also mediates signal transduction (FIGS. 3 and 7). . .

DRWD . . . NO also hyperpolarizes the cell by opening potassium channels which in turn cause closure of voltage-sensitive calcium channels. Thus, the **synergistic** interactions of calcium channel antagonists, potassium channel openers and NO donors are evident from the above signal transduction pathway.

DETD . . . anti-spasm and pain/inflammation inhibitory agents, or anti-restenosis agents from the enumerated classes, at low concentration. However, due to the aforementioned **synergistic** effect of multiple agents, and the desire to broadly block pain and inflammation, spasm and restenosis, it is preferred that. . .

DETD [0052] 5-HT.sub.1A, 5-HT.sub.1B and 5-HT.sub.1D receptors are known to inhibit adenylate cyclase activity. Thus including a **low dose** of these serotonin.sub.1A, serotonin.sub.1B and serotonin.sub.1D receptor agonists in the solution should inhibit neurons mediating pain and inflammation. The same. . .

DETD . . . acts as a vasodilator and potentiates the actions of substance P. Brain, S. D., et al., Inflammatory Oedema Induced by **Synergism** Between Calcitonin Gene-Related Peptide (CGRP) and Mediators of Increased Vascular Permeability, Br. J. Pharmacol. 99, p. 202 (1985). An example. . .

DETD [0093] **Synergistic** interactions between endothelin (ETA) antagonists and openers of ATP-sensitive potassium channels (KCOs) are expected in achieving vasorelaxation or smooth muscle. . .

DETD [0099] **Synergistic** interactions between NO donors and openers of ATP-sensitive potassium channels (KCOs) are expected to achieve vasorelaxation or smooth muscle relaxation.. . .

DETD [0105] Calcium channel antagonists, which are among the anti-spasm agents useful in the present invention, exhibit **synergistic** effect when combined with other agents of the present invention. Calcium (Ca.sup.2+) channel antagonists and nitric oxide (NO) donors interact. . .

DETD . . . on spasm of the internal mammary artery (IMA) showed that the combination of the two drugs produced a large positive

synergistic effect in the prevention of contraction (Liu et al., 1994). These studies provide a scientific basis for combination of a. . .

DETD [0107] Calcium channel antagonists also exhibit **synergistic** effect with endothelin receptor subtype A (ET.sub.A) antagonists. Yanagisawa and coworkers observed that dihydropyridine antagonists blocked effects of ET-1, an. . . and is at least partially blocked by nicardipine. Thus, the inclusion of a calcium channel antagonist would be expected to **synergistically** enhance the actions of an ET.sub.A antagonist when combined in a surgical solution.

DETD [0108] Calcium channel antagonists and ATP-sensitive potassium channel openers likewise exhibit **synergistic** action. Potassium channels that are ATP-sensitive (K.sub.ATP) couple the membrane potential of a cell to the cell's metabolic state via. . .

DETD [0109] Finally, calcium channel antagonists and tachykinin and bradykinin antagonists exhibit **synergistic** effects in mediating neuroinflammation. The role of neurokinin receptors in mediating neuroinflammation has been established. The neurokinin, (NK.sub.1) and neurokinin.sub.2. . . a common mechanism involving elevation of intracellular calcium, part of which enters through L-type channels. This is the basis for **synergistic** interaction between calcium channel antagonists and antagonists to neurokinin and bradykinin.sub.2 receptors.

DETD . . . this G-protein coupled receptor on the surface of platelet membranes. A preliminary study showed it to be more effective than **aspirin** in combination with dipyridamole. However, the clinical use of ticlopidine has been limited because it causes neutropenia. Clopidogrel, a ticlopidine. . .

DETD [0120] Agents currently utilized for conventional methods of treatment of thrombosis rely upon **aspirin**, heparin and plasminogen activators. **Aspirin** irreversibly acetylates cyclooxygenase and inhibits the synthesis of thromboxane A2 and prostacyclin. While data support a benefit of **aspirin** for PTCA, the underlying efficacy of **aspirin** is considered as only partial or modest. This is likely due to platelet activation through thromboxane A2 independent pathways that are not blocked by **aspirin** induced acetylation of cyclooxygenase. Platelet aggregation and thrombosis may occur despite **aspirin** treatment. **Aspirin** in combination with dipyridamole has also been shown to reduce the incidence of acute complication during PTCA but not the. . .

DETD [0121] Two thromboxane receptor antagonists appear to be more efficacious than **aspirin** and are believed suitable for use in the solutions and methods of the present invention. Ticlopidine inhibits both thromboxane and. . .

DETD . . . of integrelin were utilized (Topol, E., 1995 Am. J. Cardiol, 27B-33B). It was provided in combination with other agents (heparin, **aspirin**) and was shown to exhibit potent anti-platelet aggregation properties (>80%). A phase III study, the IMPACT II trial, of 4000. . .

DETD 6. **Synergistic** Interactions Derived From Therapeutic Combinations Of Anti-Restenosis Agents And Other Agents Used In Cardiovascular and General Vascular Solutions

DETD . . . appears necessary for clinical effectiveness in the therapeutic approach to vasospasm and restenosis. As described below, the rationale for this **synergistic** molecular targeted therapy is derived from recent advances in understanding fundamental biochemical mechanisms by which vascular smooth muscle cells in. . .

DETD . . . of selective inhibitors which blocks transactivation of a common signaling pathway leading to vascular smooth muscle cell

proliferation will act **synergistically** to prevent spasm and restenosis after PTCA or other cardiovascular or general vascular procedure. Specific examples are briefly detailed below.

DETD b. **Synergistic** Interactions between PKC inhibitors and Calcium Channel Antagonists

DETD [0158] In this case **synergistic** interactions among PKC inhibitors and calcium channel antagonists in achieving vasorelaxation and inhibition of proliferation occur due to "crosstalk" between. . .

DETD c. **Synergistic** Effects of PKC Inhibitors, 5-HT.sub.2 Antagonists and ET.sub.A Antagonists

DETD . . . of both 5-HT.sub.2 receptors and ET.sub.A receptors is mediated through calcium, the inclusion of a PKC inhibitor is expected to **synergistically** enhance the actions of antagonists to both of these receptors when combined in a surgical solution (see FIGS. 2 and. . .

DETD d. **Synergistic** Effects of Protein Tyrosine Kinase Inhibitors and Calcium Channel Antagonists

DETD . . . cells into a proliferative state, it is necessary to block both independent signaling arms. This is the basis for the **synergistic** interaction between calcium channel antagonists and tyrosine kinase inhibitors in the surgical solution. Because the actions of the protein tyrosine. . .

DETD e. **Synergistic** Effects of Protein Tyrosine Kinase Inhibitors and Thrombin Receptor Antagonists

DETD . . . the compounds that were reported to show selectivity for COX-2 vs. COXI, the rank order of potency was DuP 697>SC-58451, celecoxib> **nimesulide** =meloxicam=piroxicam=NS-398=RS-57067>SC-57666>SC-58125>flosulide >etodolac>L-745,337>DFU-T-614, with IC.sub.50 values ranging from 7 μM to 17 μM. A good correlation was obtained between the IC.sub.50. . .

DETD . . . of suitable COX-2 inhibitors for use in connection with the practice of the present invention include, without limitation: celecoxib, meloxicam, **nimesulide**, **nimesulide**, diclofenac, flosulide, N-[2-(cyclohexyloxy)-4-nitrophenyl]-methanesulfonamide (NS-398), 1-[(4-methylsulfonyl)phenyl]-3-trifluoromethyl-5 -[(4-fluoro)phenyl]pyrazole (SC58125), and the following compounds as described in Riendeau, D. et al., (1997). . .

	(μM)	(μM)	(μM)	(μM)
DuP 697	0.01-50,000	0.05-15,000	0.3-3,000	3-500
SC-58451	0.01-50,000	0.05-15,000	0.3-3,000	3-500
celecoxib	0.01-50,000	0.05-15,000	0.3-3,000	3-500
meloxicam	0.02-100,000	0.1-20,000	0.5-5,000	5-1,000
nimesulide	0.02-100,000	0.1-20,000	0.5-5,000	5-1,000
diclofenac	0.02-50,000	0.1-15,000	0.3-3,000	3-500
NS-398	0.01-50,000	0.06-15,000	0.3-3,000	3-500
L-745,337	0.01-150,000	0.04-50,000	0.2-10,000	2-2,000
RS57067	0.01-150,000	0.04-50,000	0.2-10,000	2-2,000

SC-58125. . .

CLM What is claimed is:

. . . method of claim 1, wherein the pharmacological agent is a COX-2 inhibitor selected from the group consisting of celecoxib, meloxicam, **nimesulide**, **nimesulide**, diclofenac, flosulide, N-[2-(cyclohexyloxy)-4-nitrophenyl]-methanesulfonamide, 1-[(4-methylsulfonyl)phenyl]-3-trifluoromethyl-5-[(4-fluoro)-phenyl]pyrazole, DuP 697, SC-58451, RS-57067, SC-57666 and L-745,337.

. . . anabaseine (GTS-21); SBI-1765F; RJR-2403; 3-((1-methyl-2(S)-pyrrolidinyl)methoxy)pyridine (A-84543); 3-(2(S)-azetidinylmethoxy)pyridine (A-85380); (+)-anatoxin-A and (-)anatoxin-A (IR)- 1 -(9-Azabicyclo [4.2.2]non-2-en-2-yl)-ethanoate fumarate, (R,S)-3-pyridyl-1-methyl-2-(3-pyridyl)azetidine (MPA), celecoxib, meloxicam, **nimesulide**, **nimesulide**, diclofenac, flosulide, N-[2-(cyclohexyloxy)-4-nitrophenyl]-methanesulfonamide, 1-[(4-methylsulfonyl)phenyl]-3-trifluoromethyl-5-[(4-fluoro)phenyl]pyrazole, DuP 697, SC-58451, RS-57067, SC-57666, L-745,337, tumor necrosis factor (TNF) soluble receptors, interleukin-1 (IL-1) cytokine. . .

IT 50-48-6, Amitriptyline 91-84-9, Mepyramine 146-48-5, Yohimbine 342-10-9, Kallidin 364-62-5, Metoclopramide 437-38-7, Fentanyl 1491-59-4, Oxymetazoline 4205-90-7, Clonidine 9087-70-1, Aprotinin 15307-86-5, Diclofenac 15585-43-0, RJR 2403 19794-93-5, Trazodone 21829-25-4, Nifedipine 33876-97-0, SIN-1 36067-72-8, BHT933 36085-73-1, BHT920 50679-08-8, Terfenadine **51803-78-2**, Nimesulide 59803-98-4, UK14304 60634-51-7, LY 53857 63675-72-9, Nisoldipine 64285-06-9, (+)-Anatoxin-A 71125-38-7, Meloxicam 74103-06-3, Ketorolac 80937-31-1, Flosulide 88149-94-4, DuP 697 91147-45-4, AGN-191103 92142-32-0 100449-06-7, A-54741 103628-46-2, Sumatriptan 113563-71-6, (R)-Pinacidil 113775-47-6, Dexmedetomidine 123653-11-2, N-[2-(Cyclohexyloxy)-4-nitrophenyl]methanesulfonamide 128270-60-0, Hirulog 129623-01-4, GR82334 133052-90-1, GF 109203X 136553-81-6, BQ 123 137431-04-0, NS-49 138472-01-2, NOR-3 138614-30-9, Hoe 140 142001-63-6, SR 48968 146535-11-7, AG1296 149017-66-3, PPADS 152121-30-7 152121-47-6 152121-53-4 155262-40-1, AGN 192172 156223-05-1, GTS-21 158205-05-1, L-745337 158959-32-1, SC-57666 161416-43-9, A 84543 161416-98-4, A-85380 161417-03-4, ABT-089 162054-19-5 162626-99-5, FR 144420 167869-21-8 168433-84-9, SC-58451 169590-42-5, Celecoxib 179382-91-3, RS-57067 188627-80-7, Integrelin 189319-35-5 198283-73-7, ABT-594 203564-57-2 340830-03-7, Receptor tyrosine kinase 402850-66-2, SBI 1765F

(irrigation solution for inhibition of pain and inflammation at wounds during surgical procedures)

L15 ANSWER 72 OF 73 USPATFULL on STN

ACCESSION NUMBER: 2002:48008 USPATFULL

TITLE: Neuroprotective, antithrombotic and anti-inflammatory uses of activated protein C (APC)

INVENTOR(S): Griffin, John H., Del Mar, CA, UNITED STATES
Zlokovic, Berislav Y., Rochester, NY, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2002028199	A1	20020307
APPLICATION INFO.:	US 2001-777484	A1	20010205 (9)

	NUMBER	DATE
PRIORITY INFORMATION:	US 2000-180227P	20000204 (60)

DOCUMENT TYPE: Utility

FILE SEGMENT: APPLICATION

LEGAL REPRESENTATIVE: Lisa A. Haile, Ph.D., Gray Cary Ware & Freidenrich LLP, 4365 Executive Drive, Suite 1600, San Diego, CA, 92121-2189

NUMBER OF CLAIMS: 21

EXEMPLARY CLAIM: 1

Jagoe

NUMBER OF DRAWINGS: 8 Drawing Page(s)
LINE COUNT: 1433
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
DRWD . . . 8A) and edema volume (FIG. 8B) in the ischemic hemisphere in mice after stroke induction treated with vehicle alone (control), **low dose** (0.1 mg/kg) of APC alone, **low dose** APC coinjected with protein S (2 mg/kg) or protein S alone. Mean±SE, from 2 to 5 animals. *p<0.05 and ns=non-significant.
DETD . . . Acid, S-Adenosylmethionine, 3-Amino-4-hydroxybutyric Acid, Amixetrine, Bendazac, Bucolome, Carbazones, Difenpiramide, Ditazol, Guaiazulene, Heterocylic Aminoalkyl Esters of Mycophenolic Acid and Derivatives, Nabumetone, **Nimesulide**, Orgotein, Oxaceprol, Oxazole Derivatives, Paranyline, Pifoxime, 2-substituted-4, 6-di-tertiary-butyl-s-hydroxy-1,3-pyrimidines, Proquazone, Sialyl Lewis.sup.x Dimers, or Tenidap. Additional therapeutic agents which can be. . .
DETD . . . those described in U.S. Pat. No. 5,679,639, incorporated by reference, can be co-administered with APC. Anti-platelet agents include, for example, **aspirin**, dipyridamole, clopidogrel, abciximab (Reopro) or any inhibitor of plately glycoprotein IIb-IIIa.
DETD [0077] In particular, it has been discovered that protein S, a co-factor of APC, has a **synergistic** effect when administered in accordance with the methods of this invention. For example, Example 3 below illustrates that administration of. . . 10-fold to 100-fold) the therapeutic dosage of APC used in the invention methods. Further, it is well known that this **synergistic** effect of the combined presence of protein S and APC is species specific, depending upon the APC and the cofactor. . .
DETD . . . described above in Example 1. Either vehicle, protein S (2 mg/kg) alone or protein S (2 mg/kg) co-injected with a **low dose** of APC (0.1 mg/kg) was injected 10 minutes after the MCA occlusion. The results shown in FIGS. 8A and 8B indicate that the **low dose** of APC alone was not protective. However, co-injection of protein S (2 mg/kg) and APC (0.1 mg/kg) produced a **synergistic** effect, significantly reducing brain infarction and edema by 71% (p<0.008) and 51% (p<0.05), respectively, in the focal brain ischemia model.
CLM What is claimed is:
18. The method of claim 16, wherein the anti-platelet agent is selected from the group consisting of **aspirin**, dipyridamole, ticlopidine, clopidogrel, abciximab (Reopro) and any inhibitor of platelet glycoprotein IIb-IIIa.

L15 ANSWER 73 OF 73 USPATFULL on STN
ACCESSION NUMBER: 2002:17247 USPATFULL
TITLE: Controlled-release compositions containing opioid agonist and antagonist
INVENTOR(S): Oshlack, Benjamin, New York, NY, UNITED STATES
Wright, Curtis, Norwalk, CT, UNITED STATES

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2002010127	A1	20020124	
	US 6716449	B2	20040406	
APPLICATION INFO.:	US 2001-781076	A1	20010208	(9)

	NUMBER	DATE

Jagoe

PRIORITY INFORMATION: US 2000-181358P 20000208 (60)
DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: DAVIDSON, DAVIDSON & KAPPEL, LLC, 485 Seventh Avenue, 14th Floor, New York, NY, 10018
NUMBER OF CLAIMS: 39
EXEMPLARY CLAIM: 1
LINE COUNT: 2654
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
SUMM [0025] In the present invention, a very **low dose** of an opioid antagonist is combined with a dose of an opioid agonist (analgesic) so as to enhance the degree. . .
SUMM . . . further include, in addition to an opioid agonist and antagonist, one or more drugs that may or may not act **synergistically** therewith. Thus, in certain embodiments, a combination of two opioid agonists may be included in the dosage form, in addition. . . also included, in addition to the opioid antagonist. Such non-opioid drugs would preferably provide additional analgesia, and include, for example, **aspirin**, acetaminophen; non-steroidal anti-inflammatory drugs ("NSAIDS"), e.g., ibuprofen, ketoprofen, etc.; N-methyl-D-aspartate (NMDA) receptor antagonists, e.g., a morphinan such as dextromethorphan or. . .
SUMM . . . include celecoxib (SC-58635), DUP-697, flosulide (CGP-28238), meloxicam, 6-methoxy-2 naphthylacetic acid (6-MNA), MK-966 (also known as Vioxx), nabumetone (prodrug for 6-MNA), **nimesulide**, NS-398, SC-5766, SC-58215, T-614; or combinations thereof. Dosage levels of COX-2 inhibitor on the order of from about 0.005 mg. . .

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(FILE 'HOME' ENTERED AT 10:24:05 ON 21 FEB 2006)

FILE 'STNGUIDE' ENTERED AT 10:24:10 ON 21 FEB 2006

FILE 'HOME' ENTERED AT 10:24:14 ON 21 FEB 2006

FILE 'REGISTRY' ENTERED AT 10:24:24 ON 21 FEB 2006
L1 1 S 50-78-2/RN
L2 1 S 51803-78-2/RN

FILE 'ADISCTI, ADISINSIGHT, ADISNEWS, BIOSIS, BIOTECHNO, CAPLUS, DDFB, DGENE, DISSABS, DRUGB, DRUGMONOG2, DRUGU, EMBAL, EMBASE, ESBIOBASE, IFIPAT, IMSDRUGNEWS, IMSPRODUCT, IPA, JICST-EPLUS, KOSMET, LIFESCI, MEDLINE, NAPRALERT, NLDB, NUTRACEUT, PASCAL, ...' ENTERED AT 10:25:32 ON 21 FEB 2006
L3 201233 S L1
L4 440667 S ASPIRIN OR ASA OR ACETYLSALICYLIC ACID
L5 444595 S L3 OR L4
L6 12543 S L2 OR NIMESULIDE
L7 2988 S L4 AND L6
L8 2380 S SUB-THERAPEUTIC
L9 19 S L8 AND L7
L10 352538 S LOW DOSE
L11 354769 S L8 OR L10
L12 159 S L7 AND L11
L13 132 DUP REM L12 (27 DUPLICATES REMOVED)
L14 749513 S SYNERG?
L15 73 S L13 AND L14

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L16          0 L15 AND @PD<1993

=> d l15 1-10 ibib, kwic

L15  ANSWER 1 OF 73  CAPLUS  COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER:         2005:340264  CAPLUS
DOCUMENT NUMBER:          142:379268
TITLE:                    Platelet aggregation inhibition by a composition
                          containing nimesulide and aspirin
                          produces a synergistic effect
INVENTOR(S):              Saeed, Sheikh Arshad; Saeed, Shahzada Omar
PATENT ASSIGNEE(S):       UK
SOURCE:                   Brit. UK Pat. Appl., 21 pp.
                          CODEN: BAXXDU
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:
```

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
GB 2407040	A1	20050420	GB 2003-24213	20031015

Jagoe

US 2005084528 A1 20050421 US 2003-718665 20031124
PRIORITY APPLN. INFO.: GB 2003-24213 A 20031015
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

TI Platelet aggregation inhibition by a composition containing **nimesulide** and **aspirin** produces a **synergistic** effect

AB A composition comprising **nimesulide** and a **sub-therapeutic** dose of **aspirin** is provided. The composition can be used as an anti-platelet aggregation agent. The anti-aggregation effect of **nimesulide** and **aspirin** preferably produces a **synergistic** effect.

ST platelet aggregation inhibition **nimesulide aspirin synergism**

IT Heart, disease
(angina pectoris; platelet aggregation inhibition by a composition containing **nimesulide** and **aspirin** produces a **synergistic** effect)

IT Heart, disease
(arrhythmia; platelet aggregation inhibition by a composition containing **nimesulide** and **aspirin** produces a **synergistic** effect)

IT Prophylaxis
(cardiovascular diseases; platelet aggregation inhibition by a composition containing **nimesulide** and **aspirin** produces a **synergistic** effect)

IT Heart, disease
(infarction; platelet aggregation inhibition by a composition containing **nimesulide** and **aspirin** produces a **synergistic** effect)

IT Platelet aggregation
Platelet aggregation
(inhibition; platelet aggregation inhibition by a composition containing **nimesulide** and **aspirin** produces a **synergistic** effect)

IT Arteriosclerosis
Cardiovascular agents
Cardiovascular system, disease
Human
Thrombosis
(platelet aggregation inhibition by a composition containing **nimesulide** and **aspirin** produces a **synergistic** effect)

IT Drug delivery systems
(rectal suppository; platelet aggregation inhibition by a composition containing **nimesulide** and **aspirin** produces a **synergistic** effect)

IT Cooperative phenomena
(**synergism**; platelet aggregation inhibition by a composition containing **nimesulide** and **aspirin** produces a **synergistic** effect)

IT Drug delivery systems
(tablets; platelet aggregation inhibition by a composition containing **nimesulide** and **aspirin** produces a **synergistic** effect)

IT Drug delivery systems
(topical; platelet aggregation inhibition by a composition containing **nimesulide** and **aspirin** produces a **synergistic**

effect)
IT **51803-78-2, Nimesulide**
RL: BSU (Biological study, unclassified); BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(platelet aggregation inhibition by a composition containing **nimesulide** and **aspirin** produces a **synergistic** effect)
IT 50-78-2, **Aspirin**
RL: BSU (Biological study, unclassified); BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**sub-therapeutic** dose of; platelet aggregation inhibition by a composition containing **nimesulide** and **aspirin** produces a **synergistic** effect)

L15 ANSWER 2 OF 73 IFIPAT COPYRIGHT 2006 IFI on STN
AN 10845812 IFIPAT;IFIUDB;IFICDB
TITLE: ANTI-PLATELET AGGREGATION COMPOSITIONS
INVENTOR(S): Saeed; Shahzada Omar, Woodford Greeen, GB
Saeed; Sheikh Arshad, Woodford Green, GB
PATENT ASSIGNEE(S): Unassigned
AGENT: BACON & THOMAS, PLLC, 625 SLATERS LANE, FOURTH FLOOR, ALEXANDRIA, VA, 22314, US

	NUMBER	PK	DATE
PATENT INFORMATION:	US 2005084528	A1	20050421
APPLICATION INFORMATION:	US 2003-718665		20031124

	NUMBER	DATE
PRIORITY APPLN. INFO.:	GB 2003-242138	20031015
FAMILY INFORMATION:	US 2005084528	20050421

DOCUMENT TYPE: Utility
Patent Application - First Publication
FILE SEGMENT: CHEMICAL
APPLICATION

NUMBER OF CLAIMS: 9
AB A combination of **nimesulide** and a **sub-therapeutic** dose of **aspirin** provides effective anti-platelet aggregation treatment.
ECLM 1. A pharmaceutical preparation comprising **nimesulide** and a subtherapeutic dose of **aspirin**.
ACLM 2. The preparation of claim 1 wherein said **nimesulide** and said **aspirin** are formulated separately for simultaneous or sequential administration.
3. The preparation of claim 1 wherein said **nimesulide** and said **aspirin** are formulated together as a single composition.
4. The preparation of claim 1 wherein said **nimesulide** and said **aspirin** are present in amounts such that the preparation has an anti-platelet aggregation effect exceeding that of either **nimesulide** or **aspirin** alone.
5. The preparation of claim 4 wherein the amounts of said **nimesulide** and said **aspirin** are such that their anti-platelet aggregation effect is **synergistic**.
6. The preparation of claim 1 wherein said **sub-therapeutic** dose of **aspirin** is 1-60 mg per dosage form.
7. The preparation of claim 1 wherein said **nimesulide** is present in an amount of 1-200 mg per dosage form.
8. The preparation of claim 1 wherein said **nimesulide** is

present in a **sub-therapeutic** amount per dosage form.
. . . need of anti-platelet aggregation treatment, said method comprising administering to said subject an effective amount of a pharmaceutical preparation comprising **nimesulide** and a **sub-therapeutic** dose of **aspirin**.

L15 ANSWER 3 OF 73 USPATFULL on STN
ACCESSION NUMBER: 2006:4524 USPATFULL
TITLE: Pyridyl-substituted porphyrin compounds and methods of use thereof
INVENTOR(S): Williams, William, Ipswich, MA, UNITED STATES
Southan, Garry, Swampscott, MA, UNITED STATES
Szabo, Csaba, Gloucester, MA, UNITED STATES

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2006003982	A1	20060105	
APPLICATION INFO.:	US 2005-90447	A1	20050325	(11)

	NUMBER	DATE	
PRIORITY INFORMATION:	US 2004-557551P	20040329	(60)
	US 2004-628465P	20041116	(60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: WILMER CUTLER PICKERING HALE AND DORR LLP, 399 PARK AVENUE, NEW YORK, NY, 10022, US
NUMBER OF CLAIMS: 101
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 15 Drawing Page(s)
LINE COUNT: 2730
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
DRWD FIG. 12 shows the effect of Compound 3 at 0.3 mg/kg/day, i.p., and **low-dose** cyclosporine (2.5 mg/kg i.p.) on rat allografts. A: untreated, B: **low-dose** cyclosporine (2.5 mg/kg), C: Compound 3 at 0.3 mg/kg/day, D: Compound 3 at 1 mg/kg/day, E: Combination of Compound 3. . .
DETD . . . case, without being bound by theory, it is believed that the Pyridyl-Substituted Porphyrin Compounds and the other therapeutic agent act **synergistically** to treat or prevent a Condition.
DETD . . . adrenocorticosteroids, such as cortisol, cortisone, fludrocortisone, prednisone, prednisolone, 6a-methylprednisolone, triamcinolone, betamethasone, and dexamethasone; and non-steroidal anti-inflammatory agents (NSAIDs), such as **aspirin**, acetaminophen, indomethacin, sulindac, tolmetin, diclofenac, ketorolac, ibuprofen, naproxen, flurbiprofen, ketoprofen, fenoprofen, oxaprozin, mefenamic acid, meclofenamic acid, piroxicam, meloxicam, nabumetone, rofecoxib, celecoxib, etodolac, and **nimesulide**.
DETD . . . therapeutic agent can be an anticancer agent. The Pyridyl-Substituted Porphyrin Compound and the other anticancer agent can act additively or **synergistically**. A **synergistic** use of a Pyridyl-Substituted Porphyrin Compound and another anticancer agent permits the use of lower dosages of one or more. . . the agents to a subject without reducing the efficacy of the agents in the treatment of cancer. In addition, a **synergistic** effect can result in the improved efficacy of these agents in the treatment of cancer and/or the reduction of adverse. . .
DETD In one embodiment, the Pyridyl-Substituted Porphyrin Compound and the anticancer agent can act **synergistically** when administered in

doses typically employed when such agents are used as monotherapy for the treatment of cancer. In another embodiment, the Pyridyl-Substituted Porphyrin Compound and the anticancer agent can act **synergistically** when administered in doses that are less than doses typically employed when such agents are used as monotherapy for the. . .

DETD A Pyridyl-Substituted Porphyrin Compound and the other therapeutic agent can act additively or, in one embodiment **synergistically** . In one embodiment a Pyridyl-Substituted Porphyrin Compound is administered concurrently with another therapeutic agent. In one embodiment a composition comprising. . .

DETD . . . above) was dissolved in 1 mL of 0.1M HCl. 10 μL of the resultant solution was injected onto a Phenomenex **Synergi** POLAR-RP HPLC column (4 μM, 80 Å, 105 mm+4.6 mm). The column was eluted at 1 mL/minute using a two-component. . .

DETD The column used for purification was packed with 345 grams of Phenomenex, **Synergi**, POLAR-RP, 10 μm particle size, 80 A pore size resin. The column dimensions were 310 mm+50 mm (diam.) and the. . .

DETD . . . resultant solution was filtered through a 0.2 μM nylon syringe filter. The filtered solution was then injected onto a Phenomenex **Synergi** POLAR-RP HPLC column (10 μM, 80 Å, 250 mm+50 mm). The column was eluted at 120 mL/minute using a two-component. . .

DETD Mice were subjected to multiple **low dose** streptozocin diabetes as previously described in J. G. Mabley et al., Br J Pharmacol., July 2001;133(6):909-19. Compound 3 (3 or. . .

L15 ANSWER 4 OF 73 USPATFULL on STN

ACCESSION NUMBER:	2006:3923 USPATFULL
TITLE:	Human tumor necrosis factor receptor TR-17
INVENTOR(S):	Ruben, Steven M., Brookville, MD, UNITED STATES Baker, Kevin P., Darnestown, MD, UNITED STATES
PATENT ASSIGNEE(S):	Human Genome Sciences, Inc., Rockville, MD, UNITED STATES (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2006003380	A1	20060105
APPLICATION INFO.:	US 2005-221849	A1	20050909 (11)

RELATED APPLN. INFO.: Division of Ser. No. US 2001-961376, filed on 25 Sep 2001, PENDING Continuation-in-part of Ser. No. US 2000-533822, filed on 24 Mar 2000, ABANDONED

	NUMBER	DATE
PRIORITY INFORMATION:	US 2000-235991P	20000926 (60)
	US 2000-254874P	20001213 (60)
	US 2000-188208P	20000310 (60)

DOCUMENT TYPE:	Utility
FILE SEGMENT:	APPLICATION
LEGAL REPRESENTATIVE:	HUMAN GENOME SCIENCES INC, INTELLECTUAL PROPERTY DEPT., 14200 SHADY GROVE ROAD, ROCKVILLE, MD, 20850, US
NUMBER OF CLAIMS:	20
EXEMPLARY CLAIM:	1
NUMBER OF DRAWINGS:	2 Drawing Page(s)
LINE COUNT:	13416

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

DETD . . . role in determining a therapeutically and/or pharmacologically

effective dosing regime. Variations of dosing such as repeated administrations of a relatively **low dose** of TR17 polypeptide for a relatively long period of time may have an effect which is therapeutically and/or pharmacologically distinguishable. . .

DETD . . . Anticoagulants that may be administered with the compositions of the invention include, but are not limited to, heparin, warfarin, and **aspirin**. In a specific embodiment, compositions of the invention are administered in combination with heparin and/or warfarin. In another specific embodiment,. . . administered in combination with warfarin. In another specific embodiment, compositions of the invention are administered in combination with warfarin and **aspirin**. In another specific embodiment, compositions of the invention are administered in combination with heparin. In another specific embodiment, compositions of the invention are administered in combination with heparin and **aspirin**.

DETD . . . Biomedix), IL-1Ra gene therapy (Valentis), JTE-522 (Japan Tobacco), paclitaxel (Angiotech), DW-166HC (Dong Wha), darbufelone mesylate (Warner-Lambert), soluble TNF receptor 1 (**synergen**; Amgen), IPR-6001 (Institute for Pharmaceutical Research), trocade (Hoffman-La Roche), EF-5 (Scotia Pharmaceuticals), BIIL-284 (Boehringer Ingelheim), BIIF-1149 (Boehringer Ingelheim), LeukoVax (Inflammatics),. . .

DETD . . . pyrazoles, pyrazolones, salicylic acid derivatives, thiazinecarboxamides, e-acetamidocaproic acid, S-adenosylmethionine, 3-amino-4-hydroxybutyric acid, amixetrine, bendazac, benzydamine, bucolome, difenpiramide, ditazol, emorfazone, guaiazulene, nabumetone, **nimesulide**, orgotein, oxaceprol, paranyline, perisoxal, pifoxime, proquazone, proxazole, and tenidap.

DETD Compounds that enhance the effects of or **synergize** with erythropoietin are also useful as adjuvants herein, and include but are not limited to, adrenergic agonists, thyroid hormones, androgens,. . .

DETD . . . pyrazoles, pyrazolones, salicylic acid derivatives, thiazinecarboxamides, e-acetamidocaproic acid, S-adenosylmethionine, 3-amino-4-hydroxybutyric acid, amixetrine, bendazac, benzydamine, bucolome, difenpiramide, ditazol, emorfazone, guaiazulene, nabumetone, **nimesulide**, orgotein, oxaceprol, paranyline, perisoxal, pifoxime, proquazone, proxazole, and tenidap.

DETD Compounds that enhance the effects of or **synergize** with erythropoietin are also useful as adjuvants herein, and include but are not limited to, adrenergic agonists, thyroid hormones, androgens,. . .

DETD . . . aureus Cowan I (SAC) or immobilized anti-hutnan IgM antibody as the priming agent. Second signals such as IL-2 and IL-15 **synergize** with SAC and IgM crosslinking to elicit B cell proliferation as measured by tritiated-thymidine incorporation. Novel **synergizing** agents can be readily identified using this assay. The assay involves isolating human tonsillar B cells by magnetic bead (MACS). . .

L15 ANSWER 5 OF 73 USPATFULL on STN

ACCESSION NUMBER:	2005:275311 USPATFULL
TITLE:	Tocopherol and tocotrienol aerosols
INVENTOR(S):	Ames, Bruce N., Berkeley, CA, UNITED STATES Jiang, Qing, Berkeley, CA, UNITED STATES
PATENT ASSIGNEE(S):	Children's Hospital & Research Center at Oakland (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2005239876	A1	20051027

Jagoe

APPLICATION INFO.: US 2005-159917 A1 20050622 (11)
RELATED APPLN. INFO.: Continuation of Ser. No. US 2002-301211, filed on 21 Nov 2002, PENDING
DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: RICHARD ARON OSMAN, SCIENCE AND TECHNOLOGY LAW GROUP, 242 AVE VISTA DEL OCEANO, SAN CLEMEMTE, CA, 92672, US
NUMBER OF CLAIMS: 21
EXEMPLARY CLAIM: 1-13
LINE COUNT: 925
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUMM Exploiting the **synergy** of the components of the medicaments, the PGE.sub.2 inhibitor may be provided at a dosage that is suboptimally therapeutic, or. . .

DETD Combinations of tocopherols and tocotrienols with dietary supplementation of omega-3 fatty acid also provide additive or **synergistic** anti-inflammatory effects. Omega-3 fatty acids, including docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA), have mild anti-inflammatory activity by way of. . .

DETD . . . therapy. COX-2 and PGE.sub.2 are elevated in inflammation-associated diseases, including cancer, and frequent intake of non-steroid anti-inflammation drugs, such as **aspirin**, reduce the risk of certain cancers. In addition to the cyclooxygenase-related mechanism, the lipoxygenase-relative pathways (one of the products of. . .

DETD Exploiting the **synergy** of the components of the medicaments, the PGE.sub.2 inhibitor may be provided at a dosage that is suboptimally therapeutic, or. . . omega-3 fatty acid cyclooxygenase substrate such as docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA).

TABLE 1

Suitable NSAID cyclooxygenase inhibitors.

Aceclofenac	N-(4-Acetamido-	**Acetylsalicylic**
acid 5-Aminosalicylic	phenyl)-indomethacin	(**aspirin**)
acid	amide	
-t-Butyl-alpha-	Celecoxib	5-Bromo-2-[4-
Diclofenac sodium		
phenylnitrone		fluorophenyl]-3-[4-(methylsulfonyl)phenyl] thiophene (DuP-697)
5,8,11,14-Eicosatetray-	8,11-eicosadiynoic	Fenoprofen (Nalfon)
Flurbiprofen		
noic acid	acid	
S(+)-Ibuprofen	Ibuprofen	Indomethacin heptyl. . .
Indomethacin		
		ester solution
Ketorolac Tris salt	Ketoprofen	S(+)-Ketoprofen
Meclofenamate		
(sodium salt)		
(S)-6-Methoxy-alpha-	(S)-6-Methoxy-alpha-	Meloxicam
Nabumetone		
methyl-2-naphthalene-	methyl-2-naphthal-	
acetic acid (Naproxen	eneacetic acid	
Sodium Salt)	(Naproxen)	

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Niflumic acid	**Nimesulide**	N-[2-(Cyclohexyloxy)-4-nitrophenyl]methanesulfonamide (NS-398) acid
Nordihydroguaiaretic		
N-(3-Pyridyl)indomethacinamide	Oxaprozin	Piroxicam
N-(2-Phenylethyl)indomethacinamide		
Phenylbutazone	Resveratrol	Rofecoxib
Sulindac sulfide		
Sulindac sulfone	Tolfenamic acid	Tolmetin
Valdecoxib		

DETD Formulation 4--Capsules. **Aspirin** and gamma-T are blended with a starch diluent in an approximate 1:3:1 weight ratio. The mixture is filled into 250 mg capsules (approx. 50 mg each of **aspirin** and 150 mg gamrna-T per capsule).

DETD Formulation 5--Capsules. **Aspirin** and delta-T are blended with a starch diluent in an approximate 1:3:1 weight ratio. The mixture is filled into 250 mg capsules (approx. 50 mg each of **aspirin** and 150 mg delta-T per capsule).

DETD Formulation 6--Capsules. **Aspirin**, gamma-T and gamma-tocotrienol are blended with a starch diluent in an approximate 1:3:3:1 weight ratio. The mixture is filled into 400 mg capsules (approx. 50 mg each of **aspirin**, 150 mg gamma-T and 150 mg gamma-tocotrienol per capsule).

DETD Formulation 11--Liquid. **Aspirin** (100 mg) and gamma-T are blended (300 mg), sucrose (1.75 g) and xanthan gum (4 mg) are blended, passed through. . .

DETD Formulation 14--Ointment. **Aspirin** and gamma-T are blended with isopropyl myristate 81 g, fluid paraffin oil 9 g and silica (Aerosil 200, 9 g,. . .

DETD Formulation 17--Non-ionic water-in-oil cream. **Aspirin** and gamma-T are blended with a mixture of emulsified lanolin 39 g alcohols, of waxes and of oils (Anhydrous eucerin,. . .

DETD Formulation 20--Lotion. **Aspirin** and gamma-T are blended with polyethylene glycol (PEG 400) 69 g and 95% Ethanol 30 g.

DETD Formulation 23--Hydrophobic ointment. **Aspirin** and gamma-T are blended with isopropyl myristate 36 g, silicone oil (Rhodorsil 36.400 g 47 V 300, Rhone-Poulenc), beeswax 13. . .

DETD . . . before the induction of inflammation. The PGE.sub.2 component of the formulation was empirically varied and adjusted to provide a minimized **synergistic** concentration. For example, **aspirin** formulations were adjusted to 50 or 100 mg/Kg with gamma-T at 30 mg/Kg. In controls evaluating the effects of aspim. . .

DETD . . . a single-center, double-blind, intra-individual, comparative study involving 18 volunteers with nickel-induced contact dermatitis. Following a positive patch test to nickel, **sub-therapeutic** amounts (10 micro 1=3 mg cm(-2)) of each of the treatments are applied twice daily for seven days to each. . .

DETD . . . the carrageenan air-pouch model, there is no casual correlation between the inhibition of PGE.sub.2 and neutrophil infiltration (11). For example, **aspirin**, at doses of 100-150 mg/kg, caused 50-70% reduction of PGE.sub.2, but yet it did not affect neutrophil infiltration (26). Although at higher doses, i.e. >200-300 mg/kg, **aspirin** inhibits cell infiltration, the mechanisms may include the inhibition of NFkB signal transduction (27) or the activation of adenosine formation. . .

DETD . . . is known that COX-2 and PGE.sub.2 are elevated in

inflammation-associated diseases including cancer (30). Frequent intake of NSAIDs such as **aspirin** is known to reduce the risk of certain cancers (31, 32). Recently, Helzlsouer et al. (33) reported that in a. . .

CLM What is claimed is:

. . . A method of inhibiting cancer cell proliferation, the method comprising the step of treating cells with a medicament comprising a **synergistic** combination of gamma-tocopherol and at least one additional phytyl substituted-chromanol selected from the group consisting of delta-tocopherol, gamma-tocotrienol, and delta-tocotrienol,. . .

21. The method of claim 14 wherein the medicament additionally comprises **aspirin**.

26. A medicament in an inhalant dosage form, the medicament comprising a combination of effective and **synergistic** amounts of gamma-tocopherol and at least one additional phytyl substituted chromanol selected from the group consisting of delta-tocopherol, gamma-tocotrienol, and. . .

33. The medicament of claim 26 that additionally comprises **aspirin**.

L15 ANSWER 6 OF 73 USPATFULL on STN

ACCESSION NUMBER:	2005:261902 USPATFULL		
TITLE:	Combination therapy comprising a Cox-2 inhibitor and an antineoplastic agent		
INVENTOR(S):	Masferrer, Jaime L., Ballwin, MO, UNITED STATES		

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2005227929	A1	20051013
APPLICATION INFO.:	US 2004-989192	A1	20041115 (10)

	NUMBER	DATE
PRIORITY INFORMATION:	US 2003-519701P	20031113 (60)

DOCUMENT TYPE:	Utility
FILE SEGMENT:	APPLICATION
LEGAL REPRESENTATIVE:	Harness, Dickey & Pierce, P.L.C., Suite 400, 7700 Bonhomme, St. Louis, MO, 63105, US
NUMBER OF CLAIMS:	20
EXEMPLARY CLAIM:	1
LINE COUNT:	12553

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUMM . . . National Cancer Inst. 94(4), 252-266. Historically, physicians have treated inflammation-related disorders with a regimen of NSAIDs such as, for example, **aspirin** and ibuprofen. Undesirably, however, some NSAIDs are known to cause gastrointestinal (GI) bleeding or ulcers in patients undergoing consistent long. . .

DETD Moreover, in certain of such embodiments, a combination therapy demonstrates **synergistic** efficacy for treating and preventing neoplasia or a neoplasia-related disorder, wherein the efficacy is greater than would be expected from. . .

DETD The phrases "**low dose**" or "**low dose** amount", in characterizing a therapeutically effective amount of a Cox-2 inhibitor or antineoplastic agent, defines a quantity that is capable. . .

DETD . . .

X is O; J is 1-phenyl; R.sup.33 is 2-NHSO.sub.2CH.sub.3; R.sup.34 is 4-NO.sub.2; and there is no R.sup.35 group (**nimesulide**);
X is O; J is 1-oxo-inden-5-yl; R.sup.33 is 2-F; R.sup.34 is 4-F; and R.sup.35 is 6-NHSO.sub.2CH.sub.3 (flosulide);
X. . .
DETD . . . consisting of celecoxib, parecoxib, deracoxib, valdecoxib, etoricoxib, meloxicam, rofecoxib, lumiracoxib, RS 57067, T-614, BMS-347070, JTE-522, S-2474, SVT-2016, CT-3, ABT-963, SC-58125, **nimesulide**, flosulide, NS-398, L-745337, RWJ-63556, L-784512, darbufelone, CS-502, LAS-34475, LAS-34555, S-33516, SD-8381, prodrugs of any of them, and mixtures thereof.
DETD . . . Bioglan
Tc-HL-91 Warwick University
solid tumor
dendritic cell cancer therapy, Cellpro Inc
neoplasm
CellPro
sandramycin analogs, Scripps Scripps Research Institute
neoplasm
colorectal tumor therapy, Nycomed **ASA**
colorectal tumor
Nycomed/TDT
antivirals, RiboGene/Trega Ribogene Inc
carcinoma
D-21621 ASTA Medica AG
neoplasm
LY-312340 Oxford University
prostate tumor, breast tumor
estradiol analogs, Pharma-Eco Pharm-Eco Laboratories. . .

L15 ANSWER 7 OF 73 USPATFULL on STN
ACCESSION NUMBER: 2005:240095 USPATFULL
TITLE: Polymer compositions and methods for their use
INVENTOR(S): Hunter, William L., Vancouver, CANADA
Toleikis, Philip M., Vancouver, CANADA
Gravett, David M., Vancouver, CANADA
Maiti, Arpita, Vancouver, CANADA
Liggins, Richard T., Coquitlam, CANADA
Takacs-Cox, Aniko, North Vancouver, CANADA
Avelar, Rui, Vancouver, CANADA
Loss, Troy A. E., North Vancouver, CANADA
PATENT ASSIGNEE(S): Angiotech International AG, Zug, SWITZERLAND (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2005208095	A1	20050922
APPLICATION INFO.:	US 2004-996354	A1	20041122 (10)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 2004-986231, filed on 10 Nov 2004, PENDING

	NUMBER	DATE
PRIORITY INFORMATION:	US 2004-586861P	20040709 (60)
	US 2004-566569P	20040428 (60)
	US 2003-526541P	20031203 (60)
	US 2003-525226P	20031124 (60)
	US 2003-523908P	20031120 (60)

Jagoe

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: SEED INTELLECTUAL PROPERTY LAW GROUP PLLC, 701 FIFTH AVENYUE, SUITE 6300, SEATTLE, WA, 98104-7092, US
NUMBER OF CLAIMS: 101
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 32 Drawing Page(s)
LINE COUNT: 34089
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

DRWD . . . and paclitaxel treated animals. FIG. 20A. Control speciment showing erosion of cartilage to the bone. FIG. 20B. Paclitaxel dose 1 (**low dose**) showing fraying of cartilage. FIG. 20C. Paclitaxel dose 2 (medium dose) showing minor defects to cartilage.

DETD . . . D-1927, D-5410, EF-13 (gamma-linolenic acid lithium salt),CMT-3 (2-naphthacenecarboxamide, 1,4,4a,5,5a,6,11,12a-octahydro-3,10,12,12a-tetrahydroxy-1,11-dioxo-, (4aS,5aR, 12aS)-), marimastat (N-(2,2-dimethyl-1(S)-(N-methylcarbamoyl)propyl)-N,3(S)-dihydroxy-2(R)-isobutylsuccinamide), TIMP'S,ONO-4817, rebimastat (L-Valinamide, N-((2S)-2-mercapto-1-oxo-4-(3,4,4-trimethyl-2,5-d ioxo-1-imidazolidinyl)butyl)-L-leucyl-N,3-dimethyl-), PS-508, CH-715, **nimesulide** (methanesulfonamide, N-(4-nitro-2-phenoxyphenyl)-), hexahydro-2-(2(R)-(1(RS)-(hydroxycarbamoyl)-4-phenylbutyl)nonanoyl)-N-(2,2,6,6-etramethyl-4-piperidinyl)-3(S)-pyridazine carboxamide, Rs-113-080, Ro-1130830, cipemastat (1-piperidinebutanamide, β-(cyclopentylmethyl)-N-hydroxy-gamma-oxo-alpha-((3,4,4-trimethyl-2,5-dioxo-1-imidazolidinyl)methyl)-,(alpha R,βR)-), 5-(4'-biphenyl)-5-(N-(4-nitrophenyl)piperazinyl)barbituric acid, 6-methoxy-1,2,3,4-tetrahydro-norharman-1-carboxylic acid, Ro-31-4724 (L-alanine, N-(2-(2-(hydroxyamino)-2-oxoethyl)-4-methyl-1-oxopentyl)-L-leucyl-, ethyl ester), prinomastat. . .

DETD . . . carbohydrates such as dextran sulfate, coumadin, coumarin, heparinoid, danaparoid, argatroban chitosan sulfate, chondroitin sulfate, danaparoid, lepirudin, hirudin, AMP, adenosine, 2-chloroadenosine, **acetylsalicylic acid**, phenylbutazone, indomethacin, meclofenamate, hydrochloroquine, dipyridamole, iloprost, streptokinase, factor Xa inhibitors, such as DX9065a, magnesium, and tissue plasminogen activator. Further examples. . .

DETD . . . from one of the following classes of compounds: anti-inflammatory agents (e.g., dexamethasone, cortisone, fludrocortisone, prednisone, prednisolone, 6α-methylprednisolone, triamcinolone, betamethasone, and **aspirin**); MMP inhibitors (e.g., batimistat, marimistat, TIMP's representative examples of which are included in U.S. Pat. Nos. 5,665,777; 5,985,911; 6,288,261; 5,952,320;. . .

DETD . . . such as imantinib, ZK-222584, CGP-52411, CGP-53716, NVP-AAK980-NX, CP-1 27374, CP-564959, PD-171026, PD-173956, PD-180970, SU-0879, and SKI-606; MMP inhibitors such as **nimesulide**, PKF-241-466, PKF-242-484, CGS-27023A, SAR-943, primomastat, SC-77964, PNU-171829, AG-3433, PNU-142769, SU-5402, and Dexlipotam; p38 MAP kinase inhibitors such as include CGH-2466. . .

DETD . . . may be further combined with anti-thrombotic and/or antiplatelet agents (for example, heparin, dextran sulfate, danaparoid, lepirudin, hirudin, AMP, adenosine, 2-chloroadenosine, **aspirin** , phenylbutazone, indomethacin, meclofenamate, hydrochloroquine, dipyridamole, iloprost, ticlopidine, clopidogrel, abcixamab, eptifibatide, tirofiban, streptokinase, and/or tissue plasminogen activator) to enhance efficacy.

DETD . . . (j) intra-arterial, (k) intracardiac, (l) transdermal, (m)

intra-ocular and (n) intramuscular. The therapeutic agent may be administered as a sustained **low dose** therapy to prevent disease progression, prolong disease remission, or decrease symptoms in active disease. Alternatively, the therapeutic agent may be. . .

DETD . . . irrigated into the joint as part of an open surgical procedure). The anti-scarring agent can be administered as a chronic **low dose** therapy to prevent disease progression, prolong disease remission, or decrease symptoms in active disease. Alternatively, the therapeutic agent can be. . .

DETD . . . of the injury (or the surgical procedure used to treat it). The anti-scarring agent can be administered as a chronic **low dose** therapy to prevent disease progression, prolong disease remission, or decrease symptoms in active disease. Alternatively, the therapeutic agent can be. . .

DETD . . . polymer compositions infiltrated into tissue adjacent to vascular graft devices can also further contain an anti-inflammatory agent (e.g., dexamethazone or **aspirin**) and/or an anti-thrombotic agent (e.g., heparin, heparin complexes, hydrophobic heparin derivatives, dipyridamole, or **aspirin**). The combination of agents may be contained in the polymer composition infiltrated into tissue adjacent to the vascular graft such. . .

DETD . . . polymer compositions infiltrated into tissue adjacent to hemodialysis access devices can also further contain an anti-inflammatory agent (e.g., dexamethazone or **aspirin**) and/or an anti-thrombotic agent (e.g., heparin, heparin complexes, hydrophobic heparin derivatives, dipyridamole, or **aspirin**).

DETD . . . may include colostomy devices, such as ASSURA Pouches and COLOPLAST Pouches, which are sold by Coloplast Corporation (Marietta, Ga.). ESTEEM **SYNERGY** Standard Closed-End Pouches and SUR-FIT NATURA Closed-End Pouches are sold by ConvaTec (Princeton, N.J.), a Bristol-Myers Squibb Company. Cymed Ostomy. . .

DETD . . . and 3487A PISCES-QUAD Quadripolar Leads made by Medtronic, Inc. (Minneapolis, Minn.). Medtronic also sells a battery-powered ITREL 3 Neurostimulator and **SYNERGY** Neurostimulator, the INTERSIM Therapy for sacral nerve stimulation for urinary control, and leads such as the 3998 SPECIFY Lead and. . .

DETD . . . to the present invention, include commercially available products. Commercially available neurostimulation devices for the management of chronic pain include the **SYNERGY**, INTREL, X-TREL and MATTRIX neurostimulation systems from Medtronic, Inc. The percutaneous leads in this system can be quadripolar (4 electrodes),. . .

DETD . . . and loss of cartilage to the bone. Bar graphs were constructed from each group and compared. Paclitaxel treatment at a **low dose** (dose 1) and medium dose (dose 2) showed a statistical reduction in cartilage damage relative to control. See FIGS. 19. . .

L15 ANSWER 8 OF 73 USPATFULL on STN
ACCESSION NUMBER: 2005:226572 USPATFULL
TITLE: Polymer compositions and methods for their use
INVENTOR(S): Hunter, William L., Vancouver, CANADA
Toleikis, Philip M., Vancouver, CANADA
Gravett, David M., Vancouver, CANADA
Maiti, Arpita, Vancouver, CANADA
Liggins, Richard T., Coquitlam, CANADA
Takacs-Cox, Aniko, North Vancouver, CANADA
Avelar, Rui, Vancouver, CANADA
Loss, Troy A E., North Vancouver, CANADA

Jagoe

PATENT ASSIGNEE(S): Angiotech International AG, Zug, SWITZERLAND (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2005196421	A1	20050908
APPLICATION INFO.:	US 2004-1417	A1	20041201 (11)

RELATED APPLN. INFO.: Continuation of Ser. No. US 2004-996354, filed on 22 Nov 2004, PENDING Continuation-in-part of Ser. No. US 2004-986231, filed on 10 Nov 2004, PENDING

	NUMBER	DATE
PRIORITY INFORMATION:	US 2004-611077P	20040917 (60)
	US 2004-586861P	20040709 (60)
	US 2004-566569P	20040428 (60)
	US 2003-526541P	20031203 (60)
	US 2003-525226P	20031124 (60)
	US 2003-523908P	20031120 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: SEED INTELLECTUAL PROPERTY LAW GROUP PLLC, 701 FIFTH AVENYUE, SUITE 6300, SEATTLE, WA, 98104-7092, US
NUMBER OF CLAIMS: 100
EXEMPLARY CLAIM: 1-7300
NUMBER OF DRAWINGS: 32 Drawing Page(s)
LINE COUNT: 34222
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

DRWD . . . and paclitaxel treated animals. FIG. 20A. Control speciment showing erosion of cartilage to the bone. FIG. 20B. Paclitaxel dose 1 (**low dose**) showing fraying of cartilage. FIG. 20C. Paclitaxel dose 2 (medium dose) showing minor defects to cartilage.

DETD . . . CH-5902, D-1927, D-5410, EF-13 (gamma-linolenic acid lithium salt),CMT-3 (2-naphthacenecarboxamide, 1,4,4a,5,5a,6,11,12a-octahydro-3,10,12,12a-tetrahydroxy-1,11-dioxo-, (4aS,5aβ,12aS)-), marimastat (N-(2,2-dimethyl-1(S)-(N-methylcarbamoyl)propyl)-N,3(S)-dihydroxy-2(R)-isobutylsuccinamide), TIMP'S,ONO-4817, rebimastat (L-Valinamide, N-((2S)-2-mercapto-1-oxo-4-(3,4,4-trimethyl-2,5-d ioxo-1-imidazolidinyl)butyl)-L-leucyl-N,3-dimethyl-), PS-508, CH-715, **nimesulide** (methanesulfonamide, N-(4-nitro-2-phenoxyphenyl)-), hexahydro-2-(2(R)-(1(RS)-(hydroxycarbamoyl)-4-phenylbutyl)nonanoyl)-N-(2,2,6,6-etramethyl-4-piperidinyl)-3(S)-pyridazine carboxamide, Rs-113-080, Ro-1130830, cipemastat (1-piperidinebutanamide, β-(cyclopentylmethyl)-N-hydroxy-gamma-oxo-alpha-((3,4,4-trimethyl-2,5-dioxo-1-imidazolidinyl)methyl)-,(alpha R,βR)-), 5-(4'-biphenyl)-5-(N-(4-nitrophenyl)piperazinyl)barbituric acid, 6-methoxy-1,2,3,4-tetrahydro-norharman-1-carboxylic acid, Ro-31-4724 (L-alanine, N-(2-(2-(hydroxyamino)-2-oxoethyl)-4-methyl-1-oxopentyl)-L-leucyl-, ethyl ester), prinomastat. . .

DETD . . . carbohydrates such as dextran sulfate, coumadin, coumarin, heparinoid, danaparoid, argatroban chitosan sulfate, chondroitin sulfate, danaparoid, lepirudin, hirudin, AMP, adenosine, 2-chloroadenosine, **acetylsalicylic acid**, phenylbutazone, indomethacin, meclofenamate, hydrochloroquine, dipyridamole, iloprost, streptokinase, factor Xa inhibitors, such as DX9065a, magnesium, and tissue plasminogen activator. Further examples. . .

DETD . . . from one of the following classes of compounds: anti-inflammatory agents (e.g., dexamethasone, cortisone,

fludrocortisone, prednisone, prednisolone, 6α-methylprednisolone, triamcinolone, betamethasone, and **aspirin**); MMP inhibitors (e.g., batimistat, marimistat-, TIIMP's representative examples of which are included in U.S. Pat. Nos. 5,665,777; 5,985,911; 6,288,261; 5,952,320;. . .

DETD . . . inhibitors, such as imantinib, ZK-222584, CGP-52411, CGP-53716, NVP-AAK980-NX, CP-127374, CP-564959, PD-171026, PD-173956, PD-180970, SU-0879, and SKI-606; MMP inhibitors such as **nimesulide**, PKF-241-466, PKF-242-484, CGS-27023A, SAR-943, primomastat, SC-77964, PNU-171829, AG-3433, PNU-142769, SU-5402, and Dexlipotam; p38 MAP kinase inhibitors such as include CGH-2466. . .

DETD . . . may be further combined with anti-thrombotic and/or antiplatelet agents (for example, heparin, dextran sulfate, danaparoid, lepirudin, hirudin, AMP, adenosine, 2-chloroadenosine, **aspirin** , phenylbutazone, indomethacin, meclofenamate, hydrochloroquine, dipyridamole, iloprost, ticlopidine, clopidogrel, abcixamab, eptifibatide, tirofiban, streptokinase, and/or tissue plasminogen activator) to enhance efficacy.

DETD . . . (j) intra-arterial, (k) intracardiac, (l) transdermal, (m) intra-ocular and (n) intramuscular. The therapeutic agent may be administered as a sustained **low dose** therapy to prevent disease progression, prolong disease remission, or decrease symptoms in active disease. Alternatively, the therapeutic agent may be. . .

DETD . . . irrigated into the joint as part of an open surgical procedure). The anti-scarring agent can be administered as a chronic **low dose** therapy to prevent disease progression, prolong disease remission, or decrease symptoms in active disease. Alternatively, the therapeutic agent can be. . .

DETD . . . of the injury (or the surgical procedure used to treat it). The anti-scarring agent can be administered as a chronic **low dose** therapy to prevent disease progression, prolong disease remission, or decrease symptoms in active disease. Alternatively, the therapeutic agent can be. . .

DETD . . . polymer compositions infiltrated into tissue adjacent to vascular graft devices can also further contain an anti-inflammatory agent (e.g., dexamethazone or **aspirin**) and/or an anti-thrombotic agent (e.g., heparin, heparin complexes, hydrophobic heparin derivatives, dipyridamole, or **aspirin**). The combination of agents may be contained in the polymer composition infiltrated into tissue adjacent to the vascular graft such. . .

DETD . . . polymer compositions infiltrated into tissue adjacent to hemodialysis access devices can also further contain an anti-inflammatory agent (e.g., dexamethazone or **aspirin**) and/or an anti-thrombotic agent (e.g., heparin, heparin complexes, hydrophobic heparin derivatives, dipyridamole, or **aspirin**).

DETD . . . may include colostomy devices, such as ASSURA Pouches and COLOPLAST Pouches, which are sold by Coloplast Corporation (Marietta, Ga.). ESTEEM **SYNERGY** Standard Closed-End Pouches and SUR-FIT NATURA Closed-End Pouches are sold by ConvaTec (Princeton, N.J.), a Bristol-Myers Squibb Company. Cymed Ostomy. . .

DETD . . . and 3487A PISCES-QUAD Quadripolar Leads made by Medtronic, Inc. (Minneapolis, Minn.). Medtronic also sells a battery-powered ITREL 3 Neurostimulator and **SYNERGY** Neurostimulator, the INTERSIM Therapy for sacral nerve stimulation for urinary control, and leads such as the 3998 SPECIFY Lead and. . .

DETD . . . to the present invention, include commercially available products. Commercially available neurostimulation devices for the management of chronic pain include the **SYNERGY**, INTREL, X-TREL

and MATTRIX neurostimulation systems from Medtronic, Inc. The percutaneous leads in this system can be quadripolar (4 electrodes),. . .

DETD . . . and loss of cartilage to the bone. Bar graphs were constructed from each group and compared. Paclitaxel treatment at a **low dose** (dose 1) and medium dose (dose 2) showed a statistical reduction in cartilage damage relative to control. See FIGS. 19. . .

L15 ANSWER 9 OF 73 USPATFULL on STN
ACCESSION NUMBER: 2005:215602 USPATFULL
TITLE: Treatment or prevention of vascular disorders with Cox-2 inhibitors in combination with cyclic AMP-specific phosphodiesterase inhibitors
INVENTOR(S): Taylor, Duncan P., Bridgewater, NJ, UNITED STATES
PATENT ASSIGNEE(S): Pharmacia Corporation, Chesterfield, MO, UNITED STATES, 63017-173 (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2005187278	A1	20050825	
APPLICATION INFO.:	US 2004-927198	A1	20040826	(10)

	NUMBER	DATE	
PRIORITY INFORMATION:	US 2003-498529P	20030828	(60)
	US 2003-513099P	20031021	(60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: James E. Davis, Harness, Dickey & Pierce, P.L.C., 7700 Bonhomme, Suite 400, Clayton, MO, 63105, US
NUMBER OF CLAIMS: 34
EXEMPLARY CLAIM: 1
LINE COUNT: 3070
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUMM Traditionally, the most commonly prescribed anti-platelet drug for the indications described above has been **aspirin**, a non-steroidal anti-inflammatory drug (NSAID). It is now recognized that many of the traditional NSAIDs are inhibitors of two cyclooxygenases,. . .

SUMM The anti-platelet effects of **aspirin** are mediated through the inhibition of the cyclooxygenase enzymes, which catalyze the synthesis of eicosanoids that are critical for platelet-vessel wall interactions. Specifically, **aspirin** exerts its anti-platelet effects through the inhibition of Cox-1-induced production of thromboxane A.sub.2, involved in platelet aggregation. See Catella-Lawson, F.,. . .

SUMM . . . effect in the treatment of other vascular disorders. Additionally, as mentioned previously, it has been shown that NSAIDs such as **aspirin** have been used in the past for treating certain vascular disorders, but it has not been reported whether a combination. . .

DETD As used herein, the terms "lowered dosages", "**low dose**", or "**low dose** amount", in characterizing a therapeutically effective amount of a Cox-2 inhibitor in combination with a cAMP-specific PDE inhibitor defines a. . .

DETD . . . to the use of either agent alone. Moreover, in preferred embodiments, the combination therapies of the present invention demonstrate a **synergistic** efficacy for treating and preventing vascular disorders and vascular disorder-related complications that is greater than what would be expected from simply combining any of the individual monotherapies. As used herein, the term "**synergistic**

Jagoe

" refers to the combination of a Cox-2 inhibitor and a cAMP-specific PDE inhibitor as a combined therapy having an efficacy. . . of vascular disorders that is greater than what would be expected merely from the sum of their individual effects. The **synergistic** effects of the embodiments of the present invention's combination therapies encompass additional unexpected advantages for the treatment and prevention of. . .

DETD . . . inhibitory activity.

TABLE 2

Additional Cox-2 Selective Inhibitors

No.	Generic Name/Compound Name	Trade Name(s)	Drug Class/Mode of Action	Dose	Manufacturer	Reference
B11	**Nimesulide**					
B12	Flosulide					
B13	NS-398					
	CAS RN 123653-11-2					
	N-(2-cyclohexyloxynitrophenyl) methane sulfonamide					Yoshimi, N. et al., in Japanese J. Cancer Res., 90(4): 406-412

. . .

DETD . . . Pharmacol. 82: 188-98

	3(2H)-pyridazinone					(2000).
A15	Pimobendan	Vetmedin	PDE-3 inhibitor and calcium sensitizer			
	Shiga, T., et al. Combined with **Low-Dose** Pimobendan in Patients with Idiopathic Dilated Cardiomyopathy and Chronic Obstructive Pulmonary Disease: Report on Two Cases.					
	(±)-4,5-dihydro-6-[2-(p-methoxyphenyl)-5-benzimidazolyl]-5-methyl-3(2H)-pyridazinone					

. . .

CLM What is claimed is:

. . . comprises at least one compound that is chosen from celecoxib, parecoxib, deracoxib, valdecoxib, rofecoxib, etoricoxib, meloxicam, rofecoxib, lumiracoxib, tilmacoxib, cimicoxib, **nimesulide**, flosulide, darbufelone, RS 57067, T-614, BMS-347070, S-2474, SVT-2016, CT-3, ABT-963, SC-58125, NS-398, L-745337, RWJ-63556, L-784512, CS-502, LAS-34475, LAS-34555, S-33516, SD-8381,. . .

. . . comprises at least one compound that is chosen from celecoxib, parecoxib, deracoxib, valdecoxib, rofecoxib, etoricoxib, meloxicam, rofecoxib, lumiracoxib, tilmacoxib, cimicoxib, **nimesulide**, flosulide, darbufelone, RS 57067, T-614, BMS-347070, S-2474, SVT-2016, CT-3, ABT-963, SC-58125, NS-398, L-745337, RWJ-63556, L-784512, CS-502, LAS-34475, LAS-34555, S-33516, SD-8381,. . .

IT 98-92-0D, Nicotinamide, benzofused-heterocyclyl derivs. 100-42-5D, Styrene, derivs. 110-00-9D, Furan, aryl derivs. 110-02-1D, Thiophene, aryl derivs. 110-86-1D, Pyridine, derivs. 123-56-8D, Succinimide, derivs. 541-59-3D, Maleimide, derivs. 2720-93-6D, 6-Phenylphenanthridine, derivs. 3713-34-6D, derivs. 11120-54-0D, Oxadiazole, derivs. 14548-01-7D, Phenanthridine-N-oxide, derivs.

27846-26-0D, Phenethylsulfone, derivs. 29925-17-5, Ro 20-1724
35838-58-5, Etazolate hydrochloride **51803-78-2**, Nimesulide
57076-71-8, Denbufylline 60719-84-8, Amrinone 61413-54-5, Rolipram
68550-75-4, Cilostamide 71125-38-7, Meloxicam 73963-72-1, Cilostazol
74150-27-9, Pimobendan 76166-55-7, Benzafentrine 77671-31-9,
Enoximone 78415-72-2, Milrinone 79855-88-2, Trequinsin 80937-31-1,
Flosulide 84243-58-3, Imazodan 85416-73-5, (S)-(+)-Rolipram
85416-75-7, (R)-(-)-Rolipram 94192-59-3, Lixazinone 97852-72-7,
Tibenelast 100643-96-7, Indolidan 101975-10-4, Zardaverine
102669-89-6, Saterinone 106730-54-5, Olprinone 115344-47-3,
Siguazodan 123653-11-2, NS-398 123663-49-0, T-614 124294-25-3
129425-83-8, ORG 9935 132210-43-6, Cipamfylline 135462-05-4, XT-44
135637-46-6, Atizoram 136145-07-8, Arofylline 139226-28-1,
Darbufelone 139482-55-6, KF19514 144035-83-6, Piclamilast
145261-31-0, ORG 20241 153259-65-5, Cilomilast 155043-84-8, T-440
158089-95-3, S 2474 158205-05-1, L-745337 162011-90-7, Rofecoxib
162054-19-5, SC-58125 162278-09-3, V11294A 162401-32-3, Roflumilast
162542-90-7, CDP840 169590-41-4, Deracoxib 179185-30-9, NSP-513
179382-91-3, RS 57067 180200-68-4, Tilmacoxib 181695-72-7, Valdecoxib
182282-60-6, D-22888 189940-24-7, Mesopram 189955-09-7, L-784512
190967-35-2, RWJ-63556 190967-35-2 191219-80-4, YM976 192767-01-4,
L 791943 197438-48-5, BMS-347070 198470-84-7, Parecoxib
202409-33-4, Etoricoxib 215122-74-0 215123-80-1 220991-20-8,
Lumiracoxib 221642-02-0 245329-99-1, CI 1018 257892-34-5, D-4418
265114-23-6, Cimicoxib 266320-83-6, ABT-963 329306-31-2, S 33516
426268-06-6, NVP-ABE171 485397-24-8, SD 8381 485397-25-9, LAS 34555
485397-26-0, LAS 34475 630395-06-1, SVT 2016 756819-21-3
756819-22-4 756819-23-5 756819-24-6 847145-69-1 847253-14-9, PAC
10649 847253-15-0, PAC 10549
(cyclooxygenase 2 inhibitor combination with cAMP-specific phosphodiesterase inhibitor for treatment or prevention of vascular disorder)

L15 ANSWER 10 OF 73 USPATFULL on STN

ACCESSION NUMBER:	2005:215464 USPATFULL
TITLE:	Polymer compositions and methods for their use
INVENTOR(S):	Hunter, William L., Vancouver, CANADA Toleikis, Philip M., Vancouver, CANADA Gravett, David M., Vancouver, CANADA Maiti, Arpita, Vancouver, CANADA Liggins, Richard T., Coquitlam, CANADA Takacs-Cox, Aniko, North Vancouver, CANADA Avelar, Rui, Vancouver, CANADA Loss, Troy A. E., North Vancouver, CANADA
PATENT ASSIGNEE(S):	Angiotech International AG, Zug, SWITZERLAND (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2005187140	A1	20050825
APPLICATION INFO.:	US 2004-408	A1	20041129 (11)
RELATED APPLN. INFO.:	Continuation of Ser. No. US 2004-996354, filed on 22 Nov 2004, PENDING Continuation-in-part of Ser. No. US 2004-986231, filed on 10 Nov 2004, PENDING		

	NUMBER	DATE
PRIORITY INFORMATION:	US 2004-586861P	20040709 (60)
	US 2004-566569P	20040428 (60)

US 2004-611077P 20040917 (60)
US 2003-526541P 20031203 (60)
US 2003-525226P 20031124 (60)
US 2003-523908P 20031120 (60)
DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: SEED INTELLECTUAL PROPERTY LAW GROUP PLLC, 701 FIFTH AVENYUE, SUITE 6300, SEATTLE, WA, 98104-7092, US
NUMBER OF CLAIMS: 103
EXEMPLARY CLAIM: 1-5846
NUMBER OF DRAWINGS: 32 Drawing Page(s)
LINE COUNT: 34103
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

DRWD . . . and paclitaxel treated animals. FIG. 20A. Control speciment showing erosion of cartilage to the bone. FIG. 20B. Paclitaxel dose 1 (**low dose**) showing fraying of cartilage. FIG. 20C. Paclitaxel dose 2 (medium dose) showing minor defects to cartilage.

DETD . . . (2R-(1(S*),2R*,3S*))--), CH-138, CH-5902, D-1927, D-5410, EF-13 (gamma-linolenic acid lithium sait),CMT-3 (2-naphthacenecarboxamide, 1,4,4a,5,5a,6,11,12a-octahydro-3,10,12,12a-tetrahydroxy-1,11-dioxo-, (4aS,5aR,12aS)-), marimastat(N-(2,2-dimethyl-1(S)--(N-methylcarbamoyl)propyl)-N,3(S)-dihydroxy-2(R)-isobutylsuccinamide), TIMP'S,ONO-4817, rebimastat(L-Valinamide, N-((2S)-2-mercapto-1-oxo-4-(3,4,4-trimethyl-2,5-dioxo-1-imidazolidinyl)butyl)-L-leucyl-N,3-dimethyl-), PS-508, CH-715, **nimesulide**(methanesulfonamide, N-(4-nitro-2-phenoxyphenyl)-), hexahydro-2-(2(R)-(1(RS)-(hydroxycarbamoyl)-4-phenylbutyl)nonanoyl)-N-(2,2,6,6-etramethyl-4-piperidinyl)-3(S)-pyridazine carboxamide, Rs-113-080, Ro-1130830, cipemastat (1-piperidinebutanamide, β-(cyclopentylmethyl)-N-hydroxy-gamma-oxo-alpha-((3,4,4-trimethyl-2,5-dioxo-1-imidazolidinyl)methyl)-,(alpha R,βR)--), 5-(4'-biphenyl)-5-(N-(4-nitrophenyl)piperazinyl)barbituric acid, 6-methoxy-1,2,3,4-tetrahydro-norharman-1-carboxylic acid, Ro-31-4724 (L-alanine, N-(2-(2-(hydroxyamino)-2-oxoethyl)-4-methyl-1-oxopentyl)-L-leucyl-, ethyl ester), prinomastat (3-thiomorpholinecarboxamide,. . .

DETD . . . carbohydrates such as dextran sulfate, coumadin, coumarin, heparinoid, danaparoid, argatroban chitosan sulfate, chondroitin sulfate, danaparoid, lepirudin, hirudin, AMP, adenosine, 2-chloroadenosine, **acetylsalicylic acid**, phenylbutazone, indomethacin, meclofenamate, hydrochloroquine, dipyridamole, iloprost, streptokinase, factor Xa inhibitors, such as DX9065a, magnesium, and tissue plasminogen activator. Further examples. . .

DETD . . . from one of the following classes of compounds: anti-inflammatory agents (e.g., dexamethasone, cortisone, fludrocortisone, prednisone, prednisolone, 6α-methylprednisolone, triamcinolone, betamethasone, and **aspirin**); MMP inhibitors (e.g., batimistat, marimistat, TIMP's representative examples of which are included in U.S. Pat. Nos. 5,665,777; 5,985,911; 6,288,261; 5,952,320;. . .

DETD . . . inhibitors, such as imantinib, ZK-222584, CGP-52411, CGP-53716, NVP-AAK980-NX, CP-127374, CP-564959, PD-171026, PD-173956, PD-180970, SU-0879, and SKI-606; MMP inhibitors such as **nimesulide**, PKF-241-466, PKF-242-484, CGS-27023A, SAR-943, primomastat, SC-77964, PNU-171829, AG-3433, PNU-142769, SU-5402, and Dexlipotam; p38 MAP kinase inhibitors such as include CGH-2466. . .

DETD . . . may be further combined with anti-thrombotic and/or antiplatelet agents (for example, heparin, dextran sulfate, danaparoid, lepirudin, hirudin, AMP, adenosine, 2-chloroadenosine, **aspirin**

, phenylbutazone, indomethacin, meclofenamate, hydrochloroquine, dipyridamole, iloprost, ticlopidine, clopidogrel, abcixamab, eptifibatide, tirofiban, streptokinase, and/or tissue plasminogen activator) to enhance efficacy.

DETD . . . (j) intra-arterial, (k) intracardiac, (l) transdermal, (m) intra-ocular and (n) intramuscular. The therapeutic agent may be administered as a sustained **low dose** therapy to prevent disease progression, prolong disease remission, or decrease symptoms in active disease. Alternatively, the therapeutic agent may be. . .

DETD . . . irrigated into the joint as part of an open surgical procedure). The anti-scarring agent can be administered as a chronic **low dose** therapy to prevent disease progression, prolong disease remission, or decrease symptoms in active disease. Alternatively, the therapeutic agent can be. . .

DETD . . . of the injury (or the surgical procedure used to treat it). The anti-scarring agent can be administered as a chronic **low dose** therapy to prevent disease progression, prolong disease remission, or decrease symptoms in active disease. Alternatively, the therapeutic agent can be. . .

DETD . . . polymer compositions infiltrated into tissue adjacent to vascular graft devices can also further contain an anti-inflammatory agent (e.g., dexamethazone or **aspirin**) and/or an anti-thrombotic agent (e.g., heparin, heparin complexes, hydrophobic heparin derivatives, dipyridamole, or **aspirin**). The combination of agents may be contained in the polymer composition infiltrated into tissue adjacent to the vascular graft such. . .

DETD . . . polymer compositions infiltrated into tissue adjacent to hemodialysis access devices can also further contain an anti-inflammatory agent (e.g., dexamethazone or **aspirin**) and/or an anti-thrombotic agent (e.g., heparin, heparin complexes, hydrophobic heparin derivatives, dipyridamole, or **aspirin**).

DETD . . . may include colostomy devices, such as ASSURA Pouches and COLOPLAST Pouches, which are sold by Coloplast Corporation (Marietta, Ga.). ESTEEM **SYNERGY** Standard Closed-End Pouches and SUR-FIT NATURA Closed-End Pouches are sold by ConvaTec (Princeton, N.J.), a Bristol-Myers Squibb Company. Cymed Ostomy. . .

DETD . . . and 3487A PISCES-QUAD Quadripolar Leads made by Medtronic, Inc. (Minneapolis, Minn.). Medtronic also sells a battery-powered ITREL 3 Neurostimulator and **SYNERGY** Neurostimulator, the INTERSIM Therapy for sacral nerve stimulation for urinary control, and leads such as the 3998 SPECIFY Lead and. . .

DETD . . . to the present invention, include commercially available products. Commercially available neurostimulation devices for the management of chronic pain include the **SYNERGY**, INTREL, X-TREL and MATTRIX neurostimulation systems from Medtronic, Inc. The percutaneous leads in this system can be quadripolar (4 electrodes),. . .

DETD . . . and loss of cartilage to the bone. Bar graphs were constructed from each group and compared. Paclitaxel treatment at a **low dose** (dose. 1) and medium dose (dose 2) showed a statistical reduction in cartilage damage relative to control. See FIGS. 19. . .